Remarks

Status of the Claims:

Claims 1-5 were originally submitted. Claims 1-5 have been finally rejected. Claims 1 and 5 are herein amended. Amended independent claims 1 and 5 and originally submitted dependent claims 2-4 are currently pending and at issue.

Support for the amendments of claim 1 and 5 may be found in the specification of the originally filed application. For example, reference to a water-in-oil topical cream may be found at page 3, lines 22-23, page 4, lines 1-4, and in the Examples.

Reconsideration is hereby respectfully requested in light of the following remarks.

Rejection Under 35U.S.C. §103

Claims 1-5 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,696,105. The '105 patent discloses a topical cream comprising (a) 0.01 to 0.25 percent Mometasone Furoate (b) 5 to 20 percent hexylene glycol (c) 1.0 to 5 percent water (d) 2.0 to 10.0 percent white wax (e) 4 to 12 percent of a lipophilic emulsifier having a HLB below 5 (f) 0.7 to 4 percent of a hydrophilic emulsifier having a HLB above 11 (g) 0.2 to 2.0 percent Titanium dioxide (h) 5 to 20 percent aluminum starch octenylsuccinate (i) 40 to 70 percent white petrolatum (j) sufficient acid to adjust the pH of the water to pH 2.5 to ±0.2. The '105 patent does not teach the viscosity or propylene glycol in a cream formulation.

The '105 patent also teaches a lotion having (a) 15 to 50% by weight propylene glycol (b) 20 to 40% by weight isopropyl alcohol (c) 20 to 60% by weight water (d) 0,1 to 3.0% by weight of a thickening agent (e) sufficient buffer to adjust the pH to between 3.0 and 6.0. The Examiner states that the range of propylene glycol given for the lotion formulation in the '105 patent would teach the range for the propylene glycol in the cream formulation of the presently pending application. The Examiner contends that it would have been obvious to one of ordinary skill in the art at the time of the invention to replace

the hexylene glycol of the known cream formulation with a propylene glycol disclosed in a general lotion formulation, and to adjust for viscosity.

When relying on a modification of prior art, it is incumbent upon the examiner to identify some suggestion to combine references or to make the modification. *In re Jones*, 958 F.2d 347, 35121 USPQ 2d 1941, 1943 (Fed. Cir. 1992) (stating that there must be some suggestion to combine "either in the references themselves or in the knowledge generally available to one of ordinary skill in the art"); see *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 292, 227 USPQ 657, 664 (Fed. Cir. 1985). An examination for unexpected results is a factual evidentiary inquiry. *In re Johnson*, 747 F.2d 1456, 1460, 223 USPQ 1260 1263 (Fed. Cir. 1984). The ultimate determination of whether an invention would have been obvious is a legal conclusion based on underlying findings of fact. Whether a reference teaches away from a claimed invention are questions of fact. *Para-Ordnance Mfg. v. SGS Importers Int'l,* 73 F.3d 1085, 1088, 37 USPQ2d 1237, 1239 (Fed. Cir. 1995). "A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. *Id* quoting *In re Gurley*, 27 F.3d, 551, 553 31 U.S.P.Q.2D (BNA) 1130, 1131 (Fed. Cir. 1994). For the following reasons, there would be no motivation for one skilled in the art to add propylene glycol to a mometasone cream formulation. Additionally, the prior art specifically teaches away from the use of propylene glycol in a mometasone cream formulation.

It is well known that corticosteroids, especially mometasone, cause vasoconstriction of the skin. Corticosteroid induced vasoconstriction of human skin is a standard clinical test for bioequivalence and efficacy (see Example 2 of presently pending application). The '105 patent teaches that the addition of propylene glycol to the lotion formulation increases the vasoconstrictive effect of mometasone. The '105 patent discloses and claims the use of mometasone on the nail surface. The accompanying vasoconstrictive effect of propylene glycol will have no effect on the nail surface, because there is no blood supply to the surface of the nail. However, increased vasoconstriction is not only an undesired side effect of steroid topical formulations, but it

also interferes with the clinical evaluation of the steroid formulations. If the excipients in the base of a steroid cream contribute to the vasoconstriction response being used as a test of bioequivalence of formulations having the same amount of steroid, then equivalent amounts of active ingredients will give different responses on the clinical test and the results will not provide for equivalence. To formulate the mometasone cream for topical application to the skin, one would not be motivated to try the propylene glycol as an excipient because, as taught by the '105 patent, propylene glycol will increase the vasoconstrictive response of the skin and the results from the clinical test could not be easily interpreted. Unexpectedly, and in contradiction to what is taught by the '105 patent, the presently pending application show that 0.1% of mometasone has an equivalent vasoconstrictive responses in the test subjects regardless of whether propylene glycol or hexylene glycol is used as a base (see Example 2).

U.S. Patent No. 4,808,610 (cited in the '105 patent at column 2, line 9, and incorporated by reference into the '105 patent) teaches that the combination of momesatone with propylene glycol resulted in a less efficacious and more irritating topical water-in-oil emulsion. Hexylene glycol is disclosed and claimed by the '610 patent to be a much more effective and less irritating skin formulation. Indeed, the '105 patent also teaches that hexylene glycol is a better base for topical formulations (column 3; lines 22-31). Thus, the prior art for mometasone topical formulations teach that propylene glycol decreases the efficacy of the mometasone and increases the unwanted side effects of skin irritation and vasoconstriction. The prior art specifically teaches away from the use of propylene glycol with mometasone cream formulations by teaching specific adverse effects of the combination.

The '105 patent teaches a mometasone lotion containing propylene glycol. The lotion, as described, is a general formula having a hydro-alcoholic base with broad ranges of ingredients. Whether the lotion is a solution or a suspension, liquid or semi-liquid, prepared fresh with each use, or a long-term stable formulation, is not discussed or claimed by the '105 application. Indeed, the '105 patent provides little more than an invitation to experiment to form a mometasone lotion. Additionally, the '105 patent

teaches that the use of propylene glycol with mometasone delivers a more potent vasoconstrictive action to skin. Additionally, the cream composition disclosed in the '105 patent is taught, by incorporation by reference of the prior art (the '610 patent), to be significantly better than a cream with propylene glycol. Thus, the prior art both provides no motivation to add propylene glycol to a mometasone cream formulation, and specifically teaches away from the combination. The independent claims of the pending application have been amended to better define the invention as a water-in-oil mometasone cream formulation containing propylene glycol. Surprisingly, the cream formulation is stable, elegant, non-irritating and useful.

Applicant respectfully contends that the currently pending claims directed to an oil-in-water mometasone cream topical composition are novel and patentable.

Conclusion

In view of the foregoing remarks and amendments, Applicant respectfully submits that the grounds of rejections stated against the claims under 35 U.S.C. §103 have been overcome and the claims are now in condition for allowance. Favorable action is earnestly solicited.

If the Examiner has any questions concerning the application, please call the Applicants' agent at 914-345-9001, ext. 6365.

Respectfully submitted,

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